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Ibuprofen Oral Suspension

General Notices

Details for the public consultation of this monograph are as follows:

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Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. **Dissolution** rotation speed updated from 50 revolutions per minute to 75 revolutions per minute. **Assay** Simplified wording for solution (1).

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Ibuprofen Oral Suspension is a suspension of *Ibuprofen* in a suitable flavoured vehicle.

The oral suspension complies with the requirements stated under Oral Liquids and with the following requirements.

Content of ibuprofen, $C_{13}H_{18}O_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Shake a quantity of the oral suspension containing 0.5 g of Ibuprofen with 25 mL of *dichloromethane* and 15 mL of *water*. Allow to stand until the layers have separated and discard the upper layer. Shake the lower layer with 5 mL of *water* and discard the upper layer. Evaporate the lower layer to dryness, add 20 mL of *water* to the residue and filter (Whatman GF/C filter is suitable). Wash the residue with 20 mL of *dichloromethane* and evaporate to dryness. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of ibuprofen *(RS 186)*.

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 75 revolutions per minute.
(b) Use 900 mL of *phosphate buffer pH 7.2*, at a temperature of 37°, as the medium.

PROCEDURE

Carry out the method for *liquid chromatography*, Appendix II D, using the following solutions.

(1) Shake the oral suspension for 30 seconds and place a volume of the oral suspension containing 0.2 g of Ibuprofen into each dissolution vessel. After 30 minutes, withdraw a sample of the medium, filter and dilute, if necessary, with the dissolution medium to produce a solution expected to contain 0.022% w/v of Ibuprofen.
(2) 0.022% w/v of *ibuprofen BPCRS* in the dissolution medium.
(3) 0.15% w/v each of *benzophenone* and *ibuprofen BPCRS* in *acetonitrile*. Dilute 1 volume to 10 volumes with the dissolution medium.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octylsilyl silica gel for chromatography* (5 µm).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

37 volumes of *acetonitrile* and 63 volumes of 0.01M *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions, the retention time of [API] is about [X] minutes.

DETERMINATION OF CONTENT

Calculate the total content of ibuprofen, $C_{13}H_{18}O_2$, in the medium using the declared content of $C_{13}H_{18}O_2$ in *ibuprofen BPCRS*.

LIMITS

The amount of ibuprofen released is not less than 75% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions immediately after preparation.

(1) Disperse with the aid of ultrasound a quantity of the oral suspension containing 0.2 g of Ibuprofen with 20 mL of *acetonitrile R1*. Add sufficient mobile phase A to produce 100 mL and filter (Whatman GF/C is suitable).
(2) Dilute 1 volume of solution (1) to 100 volumes with mobile phase A. Further dilute 1 volume to 10 volumes with mobile phase A.
(3) Dissolve 20 mg of *ibuprofen BPCRS* in 2 mL of *acetonitrile R1* , add 1 mL of a 0.006% w/v solution of *ibuprofen impurity B BPCRS* in *acetonitrile R1*, and dilute to 10 mL with mobile phase A.
(4) 0.0006% w/v of *4'-isobutylacetophenone BPCRS* (impurity E) in mobile phase A.
(5) Dissolve the contents of a vial of *ibuprofen for peak identification EPCRS* in 1 mL of *acetonitrile R1*, and dilute to 5 mL with mobile phase A.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped octadecylsilyl amorphous organosilica polymer for chromatography* (5 µm) (XTerra MS C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 214 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Mobile phase A 0.5 volume of *orthophosphoric acid*, 340 volumes of *acetonitrile R1* and sufficient *water* to produce 1000 volumes.

Mobile phase B 0.5 volume of *orthophosphoric acid*, 100 volumes of *water* and sufficient *acetonitrile R1* to produce 1000 volumes.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-25	100	0	isocratic
25-55	100→0	0→100	linear gradient
55-70	0	100	isocratic
70-71	0→100	100→0	linear gradient
71-85	100	0	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *peak-to-valley ratio* is at least 5.0, where *Hp* is the height above the baseline of the peak due to impurity B and *Hv* is the height above the baseline of the lowest point of the curve separating this peak from the peak due to ibuprofen.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of Ibuprofen in solution (2).

For the reporting threshold, use the concentration of Ibuprofen in solution (2).

For peak identification, use solution (4) and (5).

Ibuprofen retention time: about 26 minutes.

Relative retention: impurity J, about 0.2; impurity N, about 0.3; impurity A, about 0.9; impurity B, about 1.08 and impurity E, about 1.11.

LIMITS

- impurity E: not more than 0.3%;
- impurities A, J and N: not more than 0.15% of each;
- unspecified impurities: for each impurity, not more than 0.10%;
- total impurities: not more than 0.7%;
- reporting threshold: 0.05%.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions immediately after preparation.

(1) Mix a weighed quantity of the mixed oral suspension containing 0.1 g of Ibuprofen with 40 mL of *acetonitrile*, add 10 mL of 0.01M *orthophosphoric acid*, shake vigorously, dilute to 100 mL with 0.01M *orthophosphoric acid* and filter (Whatman GF/C paper is suitable).
(2) 0.1% w/v of *ibuprofen BPCRS* prepared by dissolving a suitable quantity in 40 volumes of *acetonitrile* and adding 60 volumes of 0.01M *orthophosphoric acid*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (30 cm × 3.9 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (10 µm) (µBondapak C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 2 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 220 nm.

(f) Inject 10 µL of each solution.

MOBILE PHASE

4 volumes of *acetonitrile* and 6 volumes of 0.01M *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions the retention time of ibuprofen is about 21 minutes.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral suspension, Appendix V G, and calculate the content of $C_{13}H_{18}O_2$, weight in volume, from the declared content of $C_{13}H_{18}O_2$ in *ibuprofen BPCRS*.

STORAGE

Ibuprofen Oral Suspension should be protected from light.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Ibuprofen.